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#### Abstract

The purpose of the study is to investigate dynamics across provinces and time causing Spanish pharmaceutical expenditure to increase. Adjustment for residual correlation across time periods and residual variance instability is shown to be essential. Presence of parametric instability is captured using linear time trends in the coefficients. Control for endogenous and exogenous spatial spill-over is proved to be highly important. The study adds to previous knowledge by demonstrating the fallacy of simpler traditional approaches and stresses the necessity of, not only adjusting for each of these features, but integrating them into a unified framework when analysing small-area health care data. Further, we suggest alternatives ways to resolve the problem of identifying the exogenous and endogenous spatial spill-over. While an IV approach is found to be less satisfying, the traditional approach of parametric restrictions seems adequate. Finally, an approach applying two different spatial weight matrices seems to be promising.

**Keywords:** pharmaceutical expenditure; spatial spill-over; spatial autoregression; distributed lag; identification; SUR

JEL Classifications: I11, L65, R15, C21, C23

#### 1. Introduction

During the last decade, the public pharmaceutical expenditure in Spain has grown at a rate superior to the total public health care expenditure (Darbá, 2003a, Darbá, 2003b). Thus, the public pharmaceutical expenditure makes up an increasing proportion of the total public health care expenditure. Pharmaceutical expenditure made up 16.8 percent in 1991 and had in 2002 increased to make up 23 percent of the total health care expenditure (Lopez-Casasnovas *et al.*, 2005). This growth is found not only in Spain, but is a general feature of the European Union countries (Ess *et al.*, 2003); however, with the Spanish pharmaceutical expenditure as a share of public health care expenditure exceeding EU averages (Lopez-Casasnovas, 2005). It is thus crucial to analyze the causes of this growth differential in order to focus on a rational use of medicine.

The regulation of the pharmaceutical market in Spain is shared between national regulatory bodies and the regional authorities. There are notable differences in health resources supply and health care expenditure across regions (Lopez-Casasnovas *et al.*, 2005) and there is evidence of regional variation in prescription rates and expenditure per prescription resulting in regional heterogeneity in pharmaceutical expenditure and in the pharmaceutical expenditure as a share of the total regional health care expenditure (Costa-Font and Puig-Junoy, 2004).

The studies on pharmaceutical expenditure from the regional perspective are very scant though it is possible to find a few works dealing with the analysis of the regional health care expenditure (see e.g. Kitchener *et al.*, 2003, Levaggi and Zanola, 2003, Lopez-Casasnovas and Saez, 2001, Moscone and Knapp, 2005). Despite the ample body of evidence of variations in use of procedures in the literature on small-area variation (Folland *et al.*, 2003, Ham, 1988, Joines *et al.*, 2003, Wennberg and Gittelsohn, 1973, Westert *et al.*, 2004), few studies have examined the geographical variability in use of pharmaceuticals (see e.g. Dubois *et al.*, 2002, Metge *et al.*, 1999, Morgan, 2005). The causes of

variation discussed in the literature are the prevalence of diseases, mixed opinions of the effectiveness of surgery, practice style, health supply resource and differing patient preferences.

Only a few studies of small-area variation have considered spatial variation in medical practice. Westert *et al.* (2004) studied spatial disparities in hospital discharges (measured by coefficients of variations) and found these disparities to be approximately unchanged during the 1980'es and 1990'es. Joines *et al.* (2003) found that hospitalization rates for low back problems varied significantly across the counties of North Carolina. They further found that counties with similar rates clustered geographically and concluded that spatial effects are important and should be considered in small area studies. Moscone and Knapp (2005) explored the spatial patterns of mental health expenditure and established – similar to Joines et al. – the importance of controlling for spatial spill-over. Moscone and Knapp's study found a positive significant spatial effect suggesting that adjacent local authorities mimic the behaviour of their neighbours and tend to have similar mental health expenditure. In contrast to the present study, however, none of the two latter studies considered dynamic properties as a part of their analysis.

As pooled cross sectional data are applied, the present study advocates a Seemingly Unrelated Regression (SUR) framework is in order to obtain efficient estimation. Next, it is analyzed whether the effects of determinants varies over time. It is found that this variation may be represented parsimoniously by adding interactions between a time trend and the explanatory variables to the model.

Finally, potential endogenous and exogenous spatial spill-over effects are controlled for using spatially autoregressive (SAR) and spatially distributed lag (SDL) specifications. We add further to previous practice by suggesting approaches to ensure identification of exogenous and endogenous spatial spillover in a joint model. It is found that conclusions regarding determinants of public pharmaceutical expenditure are highly sensitive to whether especially endogenous spatial spill-over is controlled for. While the exogenous spatial spill-over do play a significant role, the necessity of integrating the SAR

and SDL specifications is evident. While we find that an instrumental variable approach has less in favour of it, a joint specification with two different weight matrices seems promising.

#### 2. The Spanish pharmaceutical market

In Spain, the prices of the publicly financed pharmaceuticals are fully or partially controlled, and the price index of the medicines has practically not risen in the last decade. Nevertheless, this does not preclude that new products entering the market are introduced at a sales price higher than that of the already existing ones. Several studies have shown that the replacement of older drugs by newer, more expensive, drugs is the single most important reason for the increase in pharmaceutical expenditure (see e.g. Dubois *et al.*, 2000, Gerdtham and Lundin, 2004, Morgan, 2005), whereas the real price index of existing drugs is decreasing. The second most important reason is that a larger quantity consumed because of increases in the intensity of medication in terms of defined daily doses per patient. Similar results are found in analysis of the increasing pharmaceutical expenditure in Spain (Darbá, 2003b, Rovira *et al.*, 2001).

The Spanish national health system is a decentralized system in which the regulation of the pharmaceutical market is shared between national regulatory bodies and the regional authorities – called Autonomous Communities (AC) – however, most of the key regulatory bodies are run centrally at national level to reduce diversity and maintain overall control (Costa-Font and Puig-Junoy, 2004); see Figure 1 for a map of provinces by AC.

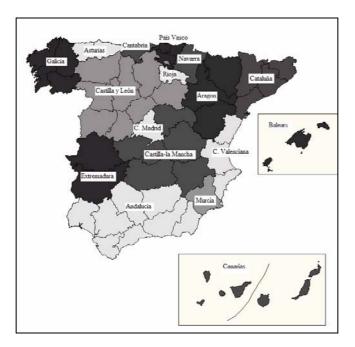


Figure 1. Provinces by AC's

Even though cost containment has been a major priority for publicly financed pharmaceuticals this has not resulted in significant savings in public expenditure (Costa-Font and Puig-Junoy, 2004, Darbá, 2003a, Darbá, 2003b). The average price for pharmaceuticals is below EU averages with older drugs priced significantly below the EU average (Puig-Junoy, 2004). The market for generic drugs was small compared to the EU average accounting for 3 percent of the market sales in 2000 and had increased to 6.4 percent by 2003 (Costa-Font and Puig-Junoy, 2004). There seems to be significant regional heterogeneity in the use of generics (Costa-Font and Puig-Junoy, 2004). New drugs are not priced significantly below the EU average and these drugs account for the largest market share (Costa-Font and Puig-Junoy, 2004, Darbá, 2003a, Darbá, 2003b). Different cost containment policies such as negative lists of excluded drugs, regulation of profits, repayments from pharmaceutical companies, reference pricing system and promotion of the use of generic drugs have had little effect on the overall increase in pharmaceutical expenditure. Some of these policies are under the devolved responsibility of the 17 regional health systems. The ACs have gradually become significant actors in the pharmaceutical

policy along with the decentralization process starting in the early 1980s until the completion of the devolution process in 2002.

Funding is mainly centrally collected and distributed to the ACs. Until 2001, the regional health care financing was decided in a separate negotiation between the Minister of Health and the corresponding Regional Ministers in the 17 ACs, mainly allocating funds as block grants following the lines of an unadjusted capitation formula (Lopez-Casasnovas *et al.*, 2005). Since 2002 the health care expenditure is allocated as part of the general financing using a capitation formula with some demographic adjustments. Health care expenditure accounts for around 40 percent of the ACs' total funding. The ACs have some possibilities of raising funding by levying higher taxes; however, various central funds strive to maintain territorial equity. There are some inter-regional inequalities in health expenditure per capita, but the coefficient of variation in regional health care expenditure may be identified (see Lopez-Casasnovas and Saez, 2001).

There seems to be significant differences in hospital specialization, physician density and technology and it has been suggested that this diversity can be partly explained by differences in particular Gross Domestic Product (GDP) and population structures (Lopez-Casasnovas *et al.*, 2005). The regional inequality in health expenditure is, however, not correlated with inequality in health outcomes (Lopez-Casasnovas *et al.*, 2005). There is evidence of significant regional variation in prescription rates and expenditure per prescription resulting in significant regional heterogeneity in pharmaceutical expenditure as a share of the total regional health care expenditure (Costa-Font and Puig-Junoy, 2004).

#### 3. Methodology

The basic linear regression model reads for one year as

(1) 
$$y_t = X_t \beta + \upsilon_t, \quad \upsilon_t \sim N(0, \sigma^2 I),$$

where  $X_t$  is an *N* by *K* dimensional matrix of explanatory variables,  $y_t$  is an *N* dimensional vector of endogenous observations,  $\beta$  is a *K* dimensional coefficient vector, and  $\upsilon_t$  is a residual with variance  $\sigma^2$ . To enable  $\beta$  to change over the years, we further add interaction variables between  $X_t$  and a time trend *T*, i.e. terms on the form  $X_t \times T$ .

Operationally, spatial spill-over in a one-period model is implemented by specifying an  $N \times N$  contiguity matrix W to summarize the spill-over between provinces. Traditional choices are the first order neighbourhood matrix obtained by letting  $w_{ij}$  equal 1 if provinces i and j are neighbours ( $i \neq j$ ) and 0 otherwise. A second, but less frequently applied approach is to let  $w_{ij}$  equal the reciprocal distance between provinces i and j ( $i \neq j$ ), while  $w_{ii}$  is set to 0. In both cases, each element out of the diagonal in W is divided with the sum of the elements in the row it belongs to. Thus, the product  $Wy_i$  defines a variable, which for each province holds a weighted average of  $y_i$  in the remaining municipalities. For the case of the first-order neighbourhood matrix, the simple average of  $y_i$  in the neighbouring provinces is obtained, while for the reciprocal distance matrix a weighted sum over all regions (each weighted inversely by distance to region i) occurs.

The endogenous spatial spill-over is captured by a spatially autoregressive (SAR) specification on the form (Anselin, 1988)

(2) 
$$y_t = \lambda(W_1 y_t) + X_t \beta_t + \upsilon_t,$$

where  $\lambda$  is a parameter specifying the degree of spill-over, formally restricted to the interval between (-1) and (+1), but for most practical purposes restricted to be non-negative, and  $W_1$  any of the above described weight matrices. Likewise, exogenous spatial spill-over is captured by enlarging the linear specification with spatial lags of  $X_i$  to obtain the Spatial Distributed Lag (SDL) specification (Florax, 1992)

(3) 
$$y_t = X_t \beta_t + (W_2 X_t) \delta + \upsilon_t,$$

where  $W_2$  is any of the weight matrices described above. By combining (2) and (3), a SAR-SDL may be obtained. However, one must here be aware of a potential identification problem. Specifically, the parameters of the SAR-SDL are only identified if  $W_1$  and  $W_2$  are different. If they are equal, the indirect effect of  $W_2X_t$  on  $y_t$  (via  $W_1y_t$  through the SAR term) interferes with the direct effect of  $W_2X_t$  on  $y_t$ (cf. Manski, 1993). The problem is illustrated in Figure 2 with  $W_1 = W_2 = W$ .

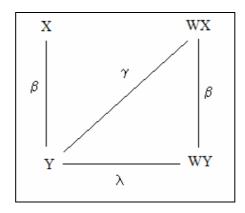


Figure 2. The identification problem

An obvious way of circumventing the problem is to impose parametric restrictions. Trivial solutions are to restrict  $\lambda = 0$  or  $\delta = 0$  thus returning to the SDL or the SAR respectively. A further solution is to impose the Durbin restriction  $\delta = -\lambda\beta$ , which essentially leads to a spatially autocorrelated residuals (SAC) specification (Anselin, 1988), which is equivalent to (1) but with the residual specification

(4) 
$$\upsilon_t = \lambda W \upsilon_t + \varepsilon_t$$

A second obvious solution is to apply two different weight matrices. However, as it may potentially be problematic to advocate the parametric restrictions as well as allocation of matrices to processes, we suggest an alternative Two-Stage Least Squares (2SLS) instrumental approach, which may be applicable for only one weight matrix and which circumvents the subjectivity of imposing parametric restrictions.

Specifically, we suggest replacing  $Wy_t$  with the predicted values  $W\hat{y}_t$  from an initial regression of  $Wy_t$ on those variables of  $WX_t$  which were not significant in the SDL. These latter variables were next omitted from the SAR-SDL. The idea is illustrated in Figure 3.

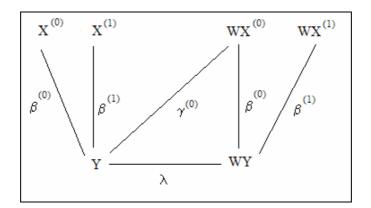


Figure 3. An identified SAR-SDL

Further, when applying pooled data for T years, the residuals are inter-correlated across years, and the variances within years vary over time, i.e. a set of T seemingly unrelated regressions (SUR) occurs. Thus, the residual covariance matrix between any two years read as

(5) 
$$E(\upsilon_t \upsilon_s') = \sigma_{ts}^2 I_N \quad t, s = 1,..,T$$

While the SDL-SUR specification can be consistently estimated using the Zellner (1962) Feasible Generalised Least Squares (F-GLS) approach by simply adding ( $WX_t$ ) to the explanatory variables, the SAR-SUR cannot be estimated consistently by F-GLS due to the contemporaneous correlation among the observations in  $y_t$  (Anselin, 1988). Consistent estimates were obtained using the following Maximum Likelihood approach: We did a grid search of the relevant values of  $\lambda$  from -1 to +1. Conditioned on each value of  $\lambda$ , F-GLS were performed using ( $y_t - \lambda Wy_t$ ) instead of  $y_t$ , and the set of results which maximized the log likelihood function (Anselin, 1988) were selected. The same procedure readily applies to the two-matrix as well as the instrumental approach SAR-SDL-SUR.

To provide devices for comparison of alternative models, some quantities are applied. One is a pseudo-R-square ( $R^2$ ), calculated as the square of the correlation between y and its predicted values. This measure is readily calculated for the SUR, the SDL-SUR and the SAC-SUR models, but is not defined for the SAR-SUR and the SAR-SDL-SUR specifications. A second device applied is the familiar Akaike Information Criterion (AIC). Finally, a Likelihood Ratio (LR) test, which is calculated for each of the spatially adjusted models versus the baseline spatially unadjusted SUR, serves as a device for comparison of models.

#### 4. Data

Data for 50 Spanish provinces were collected. These provinces correspond with the NUT-3 level of aggregation according to EUROSTAT<sup>1</sup>. The provinces are assembled in 17 Autonomous Communities (AC). The ACs correspond with the NUT-2 level of aggregation according to EUROSTAT and they present a higher degree of heterogeneity than the provinces. Regarding the decentralisation process, 7 of the ACs got independent responsibilities during the 1980's and 1990's<sup>2</sup>, while the last 10 got responsibilities for health care regulation in 2002. Until then these 10 ACs were centrally regulated.

<sup>&</sup>lt;sup>1</sup> Excluding the autonomous cities of Ceuta and Melilla.

<sup>&</sup>lt;sup>2</sup> Cataluña (1981), Andalucía (1984), Comunidad Valenciana y País Vasco (1987), Galicia y Navarra (1991) and Canarias (1994).

ta applied for the study				
Description	Source	Mean	Std. D.	
Pharmaceutical Expenditure per capita	MSC, Inst. of Sanitary Information	164.899	31.710	
GDP per capita	INE, National Statistical Inst.	9241.57	1766.14	
Pharmacists per 1000 inhabitants	INE, Social Indicators, 2004	1.206	0.225	
Hospital beds per 1000 inhabitants	MSC, National Hospital Catalogue	0.004	0.001	
Medical doctors per 1000 inhabitants	INE, Social Indicators, 2004	4.183	0.739	
Population proportion of females	n proportion of females INE, National Statistical Inst.			
Population proportion of foreigners	ulation proportion of foreigners INE, National Statistical Inst.		0.019	
Population proportion over 65 years	INE, National Statistical Inst.	0.185	0.042	
Population proportion from 0 to 4 years	INE, National Statistical Inst.	0.090	0.016	
	DescriptionPharmaceutical Expenditure per capitaGDP per capitaPharmacists per 1000 inhabitantsHospital beds per 1000 inhabitantsMedical doctors per 1000 inhabitantsPopulation proportion of femalesPopulation proportion of foreignersPopulation proportion over 65 years	DescriptionSourcePharmaceutical Expenditure per capitaMSC, Inst. of Sanitary InformationGDP per capitaINE, National Statistical Inst.Pharmacists per 1000 inhabitantsINE, Social Indicators, 2004Hospital beds per 1000 inhabitantsMSC, National Hospital CatalogueMedical doctors per 1000 inhabitantsINE, Social Indicators, 2004Population proportion of femalesINE, National Statistical Inst.Population proportion of foreignersINE, National Statistical Inst.Population proportion over 65 yearsINE, National Statistical Inst.	DescriptionSourceMeanPharmaceutical Expenditure per capitaMSC, Inst. of Sanitary Information164.899GDP per capitaINE, National Statistical Inst.9241.57Pharmacists per 1000 inhabitantsINE, Social Indicators, 20041.206Hospital beds per 1000 inhabitantsMSC, National Hospital Catalogue0.004Medical doctors per 1000 inhabitantsINE, Social Indicators, 20044.183Population proportion of femalesINE, National Statistical Inst.0.506Population proportion of foreignersINE, National Statistical Inst.0.018Population proportion over 65 yearsINE, National Statistical Inst.0.185	

The data were collected annually from 1996 to 2003 from two sources, The National Statistical Institute (INE) and the Ministry of Health and Consumption (MSC). The dependent variable is Public Pharmaceutical Expenditure (EXP) per capita. This variable includes the expenditure on extra-hospital drugs managed by the administration, but does not take private purchase into account. To capture influence of wealth, Gross Domestic Product per capita (GDP) is included as an explanatory variable. Further, to capture influence of health care system, the variables number of pharmacists per 1000 inhabitants (PHARM), number of hospital beds per 1000 inhabitants (BEDS), and number of medical doctors per 1000 inhabitants (MED) are included. Finally, to capture influence of population structure, population proportions of females (FEM), foreigners (FOREIGN), people over 65 years (OLD), and 0-4 year old children (CHILD) are included. Table 1 presents the data applied, including means and standard deviations (average over eight years).

The variables describing the population control for socio-demographic risk factors and are considered to be proxies for need, whereas GDP controls for ability to pay. The variables describing the health care system do not solely reflect supply factors but are a result of an interaction between demand and supply factors. Some health system variables may be considered to be substitutes of utilization of

pharmaceuticals while others are complementary. A priori, one would expect the number of pharmacists to be complementary, whereas we have no unambiguous a priori hypothesis for hospital beds and medical doctors.

Figure 4 shows the distribution of variables (average over eight years) by provinces. Spatial patterns are predominant, though not of a unique nature. For the expenditure, a clear indication of spatial spill-over is seen. Comparing the maps in Figure 4 to the map of ACs in Figure 1, this spill-over seems to be of an intra- as well as a supra-AC nature. Further, there seems to be some tendencies to North/West-South/East contrasts. With respect to GDP, medical doctors, hospital beds and, to some extent, pharmacists, a clear North-South contrast is evident. This is also the case for some of the population characteristics, especially elderly, children and to some extent females, while foreigners seem to cluster especially over the East coast provinces.

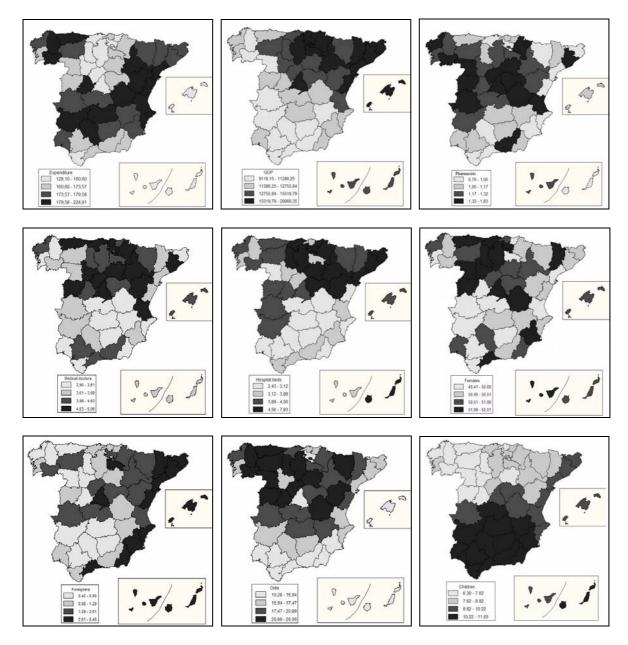


Figure 4. Variables (average over eight years) by province

## 5. Results

The model estimated is a multiplicative Cobb-Douglas type specification, which is linearized by applying log-log transforms of the variables. An initial SUR model with common coefficients, a time trend (T) and interactions between T and the explanatory variables appears in the first column of Table 2. The adequacy of this model is supported by the rather high pseudo- $R^2$ .

	Isted and spatially adjusted SUR models   [1] [2] [3] [4] [5] [6]						
	SUR	SAR-SUR	SAR-SUR	SDL-SUR	SAR-SDL-SUR	SAR-SDL-SUR	
		$(W_{\rm N})$	$(W_{\rm D})$	$(W_{\rm N})$	$(W_{\rm D})$ - $(W_{\rm N})$	(IV)	
Constant	7.075***	3.281***	2.552***	8.986***	4.296***	8.423***	
	(0.673)	(0.603)	(0.665)	(0.864)	(0.929)	(0.783)	
GDP	0.042	0.024	0.051	0.077**	0.086**	0.064*	
	(0.035)	(0.030)	(0.033)	(0.040)	(0.034)	(0.033)	
PHARM	0.018	0.062**	0.039	0.016	0.043	0.017	
	(0.034)	(0.031)	(0.032)	(0.037)	(0.032)	(0.033)	
BEDS	0.001	-0.009	0.010	-0.016	-0.006	-0.013	
(55	(0.016)	(0.015)	(0.016)	(0.017)	(0.015)	(0.015)	
MED	0.061	0.062*	0.041	0.056	0.031	0.057	
	(0.039) 1.832***	(0.035)	(0.038)	(0.039) 0.606	(0.037)	(0.036)	
FEM	-	0.943	1.773***		0.688	0.743	
CODEICN	(0.673) 0.012**	(0.607)	(0.670)	(0.714)	(0.684)	(0.680)	
FOREIGN		0.002	0.001	0.009	0.002	0.009	
OLD	(0.006) 0.212***	(0.006) 0.144***	(0.006) 0.170***	(0.006) 0.160***	(0.006) 0.157***	(0.006) 0.155***	
JLD	(0.055)	(0.049)	(0.055)	(0.059)	(0.058)	(0.054)	
CHILD	0.175***	0.078**	0.143***	0.169***	0.135***	0.159***	
	(0.045)	(0.039)	(0.045)	(0.048)	(0.045)	(0.044)	
Т	0.118	0.008	0.035	0.208***	0.127*	0.189***	
1	(0.073)	(0.069)	(0.078)	(0.075)	(0.076)	(0.070)	
T×GDP T×PHARM	-0.020***	-0.009**	-0.015***	-0.024***	-0.021***	-0.022***	
	(0.004)	(0.004)	(0.004)	(0.006)	(0.004)	(0.004)	
	0.008*	0.002	0.009*	0.005	0.005	0.005	
	(0.004)	(0.004)	(0.005)	(0.005)	(0.004)	(0.004)	
T×BEDS	0.002	0.004	-0.001	0.005*	0.003	0.004	
IXDEDS	(0.003)	(0.003)	(0.003)	(0.003)	(0.003)	(0.003)	
T×MED	-0.013**	-0.009*	-0.008	-0.012**	-0.007	-0.011**	
INNED	(0.005)	(0.005)	(0.006)	(0.006)	(0.005)	(0.005)	
T×FEM	-0.090	-0.108*	-0.127*	0.006	-0.049	-0.002	
	(0.064)	(0.059)	(0.068)	(0.067)	(0.065)	(0.061)	
T×FOREIGN	0.001	0.001	0.001	0.001	0.001	-0.001	
	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	
T×OLD	0.002	0.009*	0.005	0.002	0.006	0.003	
	(0.006)	(0.005)	(0.006)	(0.006)	(0.006)	(0.005)	
T×CHILD	-0.032***	-0.013*	-0.024***	-0.035***	-0.025***	-0.033***	
	(0.007)	(0.006)	(0.008)	(0.009)	(0.008)	(0.007)	
λ		0.651***	0.872***		0.877***	0.037***	
		(0.003)	(0.005)		(0.004)	(0.002)	
W×GDP W×PHARM W×BEDS W×MED W×FEM W×FOREIGN W×OLD				-0.022	-0.045	(IV)	
				(0.053)	(0.049)		
				0.217***	0.146***	0.214***	
			-	(0.062)	(0.050)	(0.051)	
				-0.032	-0.039**	(IV)	
				(0.022)	(0.020)	0.4.0 2 databate	
				-0.121**	-0.039	-0.129***	
			+	(0.053)	(0.048)	(0.050) 2.682***	
				2.018***			
	1			(0.845) 0.040***	(0.825) 0.029***	(0.795) 0.039***	
				(0.009)	(0.009)	(0.009) (IV)	
				0.038 (0.090)	-0.036 (0.084)	(1V)	
W×CHILD							
				0.091 (0.064)	0.102*	(IV)	
	1367.88	1420.06	1421.28	1380.38	(0.060) 1430.56	1378.38	
LogL AIC	-2625.76	-2730.13	-2732.55	-2636.79	-2735.13	-2636.79	
$\frac{AIC}{R^2}$	-2625./6	-2/30.13	-2/32.33	0.80	-2/33.13	-2030./9	
	0./8	104.36***	106.80***	25.00***	175 2/***	21.84***	
LR [2-6] vs. [1]			(***), 5% (**) and 3		125.36***	21.04	

GDP is found to have a positive impact on expenditure, but the effect is significantly reduced over time (cf. T×GDP) and will even be negative after two years. Turning to characteristics of health care system, pharmacists is found to have an increasing (cf. T×PHARM), but weakly significant, positive effect on expenditure. Hospital beds is insignificant, while medical doctors has an insignificant positive effect, which is significantly reduced over time (cf. T×MED). Regarding population characteristics, females and old people exert positive effects on expenditure, which do not change significantly over time. The number of children has a positive impact on expenditure, but this effect is seen to be significantly reduced over time (cf. T×CHILD). Finally, the time trend seems to be insignificant (cf. T).

Next, the presences of endogenous and exogenous spatial spill-over effects are considered. The second and third column of Table 2 reports two variants of the SUR model enlarged with endogenous spillover effects, i.e. the SAR-SUR specification, where the first order neighbourhood matrix and the reciprocal distance matrix are applied respectively. The specification with the reciprocal distance matrix is the optimal of these and will be extended with exogenous lags to a SAR-SDL-SUR specification. According to the discussion under Methodology, we suggest two variants, which are both identified: The first one (column 5) elaborates on the SAR with reciprocal distance weight matrix by applying the first order neighbourhood matrix for the WX terms. The second specification (column 6) is an instrumentalised version, with the first order neighbourhood matrix applied to Wy as well as WX, as we exclude these terms from WX which were insignificant in a SDL-SUR, and use these to instrumentalise Wy. To provide the basis for this division of the WX variables, we estimated the SDL-SUR (column 4). The coefficient for the spatial endogenous lag (W×EXP) is large and highly significant. The AIC is better for this model than for the unadjusted SUR (1). Further, the LR test for models (2) and (3) versus (1) significantly rejects the unadjusted SUR in favour of the SAR-SUR. It is thus evident that the pharmaceutical market is of a large area or supra-provincial nature, and that potential policy opportunities of a small area province are overestimated if endogenous spatial spill-over is not

controlled for. Further, the impact of the determinants varies substantially across the two models. When controlling for endogenous spatial spill-over, the effect of GDP and the time trend (T) in this effect are reduced to about half of the effects obtained from the unadjusted SUR. The effect of pharmacists is almost multiplied by four and turns from insignificant to significant, while its time trend is substantially reduced and looses any indication of significance. For hospital beds, the coefficient as well as its time trend is still insignificant. The effect of medical doctors as well as its time trend is practically unchanged. For the population structure variables, the effects are drastically reduced. Regarding the time trends of the latter effects, a substantial increase for old people and a substantial decrease for children are found, while the time trends of the effects of females and foreigners are practically unchanged.

The SAR-SDL-SUR was estimated applying the inverse distance matrix to the SAR term and the neighbourhood matrix to the SDL. The LR test of this specification as well as the AIC as compared to the relevant SAR-SUR (3) indicates that the additional SDL terms represent a significant improvement.

Finally, concerning the instrumentalised SAR-SDL-SUR, the variables W×GDP, W×BEDS, W×OLD and W×CHILD (occurring to be insignificant in the SDL-SUR) were applied as instruments for W×EXP. Turning to the AIC values, this model seems to fit better than the unadjusted SUR (1) model and the SDL-SUR (3) model, but poorer than any of the SAR-SUR models (2)-(3). Further, the large difference in the estimated  $\lambda$  value as compared to the SAR-SUR gives rise to questioning the reliability of the instrumentalisation.

#### 6. Conclusions

The study investigated dynamics across provinces and time causing Spanish pharmaceutical expenditure to increase. Adjustment for residual correlation across time periods and residual variance instability was shown to be essential. Control for endogenous and exogenous spatial spill-over was proved to be highly important. The study added to previous knowledge by demonstrating the fallacy of simpler traditional

approaches and stressing the necessity of, not only adjusting for each of these features, but integrating them into a unified framework when analysing small-area health care data. Further, we suggested alternative ways to resolve the problem of identifying the exogenous and endogenous spatial spill-over. While an IV approach was found to be less satisfying, the traditional approach of parametric restrictions seemed adequate. Finally, an approach applying two different spatial weight matrices seemed to be promising.

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